

Appendix A  
ASSIGNMENT

Ve, Roger Frechette, of Reading, Massachusetts, Peter Viski, of Brookline, Massachusetts, Todd E. Sawyer, of Charlton, Massachusetts, Karen Stapleton, of Weymouth, Massachusetts, Paul Hawkins, of Cambridge, Massachusetts, Beena Bhatia, of Arlington, Massachusetts, Atul Verma, of Arlington, Massachusetts, Laura McIntyre, of Cambridge, Massachusetts, and Tadeusz Warchol, of Acton, Massachusetts in consideration of One Dollar and other valuable consideration paid to us by

PARATEK PHARMACEUTICALS, INC.

a corporation of Delaware, having its principal place of business at 75 Kneeland Street, Boston, MA 02111, the receipt of which is hereby acknowledged, do hereby sell, assign and transfer unto said

PARATEK PHARMACEUTICALS, INC.

its successors and assigns, the entire interest for the United States of America and all foreign countries including all rights of priority under the International Convention for the Protection of Industrial Property in a certain invention or improvement in

9- SUBSTITUTED MINOCYCLINE COMPOUNDS

described in an application

- ☐ executed by us of even date herewith and about to be filed  
☒ Serial No. 09/895,857, filed on June 29, 2001

in the United States Patent and Trademark Office, and in all Letters Patent of the United States and all foreign countries which may or shall be granted on said invention, or any parts thereof, or on said application, or any divisional, continuing, reissue or other applications based in whole or in part thereon. And we agree, for ourselves and our executors and administrators, with said corporation and its successors and assigns but at its or their expense and charges, hereafter to execute all applications, amended specifications, deed or other instrument, and to do all acts necessary or proper to secure the grant of Letters Patent in the United States and in all other countries to said corporation, with specifications and claims in such form as shall be approved by the counsel of said corporation and to vest and confirm in said corporation, its successors and assigns, the legal title to all such patents.

And we do hereby authorize and request the Commissioner of Patents and Trademarks of the United States to issue such Letters Patent as shall be granted upon said application or applications based thereon to said corporation, its successors and assigns.

WITNESS my hand and seal this \_\_\_\_\_ day of \_\_\_\_\_, 2001.

By: Roger Frechette  
Roger Frechette

Commonwealth of Massachusetts )  
County of Middlesex )ss

Then personally appeared the above named Roger Frechette and acknowledged the foregoing instrument to be his free act and deed, before me, this day of Oct 11, 2001.

Adriana Ortiz  
Notary Public

My commission expires: Nov 17 2006

WITNESS my hand and seal this 27 day of February, 2002.

By: Peter Viski  
Peter Viski

Commonwealth of Massachusetts )  
 )ss  
County of Middlesex )

Then personally appeared the above named Peter Viski and acknowledged the foregoing instrument to be his free act and deed, before me, this 27 day of February, 2002.

Lauren M. Hammond  
Notary Public

My commission expires: \_\_\_\_\_

LAUREN M. HAMMOND  
Notary Public  
My Commission Expires  
June 23, 2006

WITNESS my hand and seal this \_\_\_\_\_ day of \_\_\_\_\_, 2002.

By: \_\_\_\_\_  
Todd E. Bowser

Commonwealth of Massachusetts )  
 )ss  
County of \_\_\_\_\_ )

Then personally appeared the above named Todd E. Bowser and acknowledged the foregoing instrument to be his free act and deed, before me, this day of \_\_\_\_\_, 2002.

\_\_\_\_\_  
Notary Public

My commission expires: \_\_\_\_\_

WITNESS my hand and seal this \_\_\_\_\_ day of \_\_\_\_\_, 2001.

By: \_\_\_\_\_  
Peter Viski

Commonwealth of Massachusetts )  
 )ss  
County of )

Then personally appeared the above named Peter Viski and acknowledged the foregoing instrument to be his free act and deed, before me, this \_\_\_\_\_ day of \_\_\_\_\_, 2001.

\_\_\_\_\_  
Notary Public

My commission expires: \_\_\_\_\_

WITNESS my hand and seal this 3rd day of October, 2001.

By: Todd E. Bowser  
Todd E. Bowser

Commonwealth of Massachusetts )  
 )ss  
County of Middlesex )

Then personally appeared the above named Todd E. Bowser and acknowledged the foregoing instrument to be his free act and deed, before me, this day of Oct 14, 2001.

Adrian Oster  
Notary Public

My commission expires: Nov. 17, 2006

WITNESS my hand and seal this 20 day of October, 2001.

By: Karen Stapleton  
Karen Stapleton

Commonwealth of Massachusetts )  
County of Norfolk )ss  
)

Then personally appeared the above named Karen Stapleton and acknowledged the foregoing instrument to be her free act and deed, before me, this 11 day of October, 2001.

Aldrin Ortiz  
Notary Public

My commission expires: Nov 17 2006

WITNESS my hand and seal this \_\_\_\_\_ day of \_\_\_\_\_, 2001.

By: \_\_\_\_\_  
Paul Hawkins

Commonwealth of Massachusetts )  
County of \_\_\_\_\_ )ss  
)

Then personally appeared the above named Paul Hawkins and acknowledged the foregoing instrument to be his free act and deed, before me, this \_\_\_\_\_ day of \_\_\_\_\_, 2001.

\_\_\_\_\_  
Notary Public

My commission expires: \_\_\_\_\_

By: Karen Stapleton

Sharon Mehn  
Notary Public

By: Paul Hawkins  
Paul Hawkins

---

**Notary Public**

My commission expires:

WITNESS my hand and seal this 3 day of October, 2001.

By: Beena Bhatia  
Beena Bhatia

Commonwealth of Massachusetts )  
County of Middlesex )ss  
)

Then personally appeared the above named Beena Bhatia and acknowledged the foregoing instrument to be her free act and deed, before me, this 11 day of October, 2001.

Adrian Ortiz - Not.  
Notary Public

My commission expires: Nov 17 2006

WITNESS my hand and seal this 4<sup>th</sup> day of October, 2001.

By: Atul Verma  
Atul Verma

Commonwealth of Massachusetts )  
County of Middlesex )ss  
)

Then personally appeared the above named Atul Verma and acknowledged the foregoing instrument to be his free act and deed, before me, this 11 day of October, 2001.

Adrian Ortiz - Not.  
Notary Public

My commission expires: Nov 17, 2006

WITNESS my hand and seal this 9<sup>th</sup> day of October, 2001.

By: Laura McIntyre  
Laura McIntyre

Commonwealth of Massachusetts )  
County of Middlesex )ss  
)

Then personally appeared the above named Laura McIntyre and acknowledged the foregoing instrument to be her free act and deed, before me, this 11 day of October, 2001.

Adrianna Ortiz Zest  
Notary Public

My commission expires: Nov 17 2006

WITNESS my hand and seal this 9 day of October, 2001.

By: Tadeusz Warchol  
Tadeusz Warchol

Commonwealth of Massachusetts )  
County of Middlesex )ss  
)

Then personally appeared the above named Tadeusz Warchol and acknowledged the foregoing instrument to be his free act and deed, before me, this 11 day of October, 2001.

Adrianna Ortiz Zest  
Notary Public

My commission expires: Nov. 17 2006

ASSIGNMENT

I, David Messersmith, of Somerville, Massachusetts in consideration of One Dollar and other valuable consideration paid to me by

PARATEK PHARMACEUTICALS, INC.

a corporation of Delaware, having its principal place of business at 75 Kneeland Street, Boston, MA 02111, the receipt of which is hereby acknowledged, do hereby sell, assign and transfer unto said

PARATEK PHARMACEUTICALS, INC.

its successors and assigns, the entire interest for the United States of America and all foreign countries including all rights of priority under the International Convention for the Protection of Industrial Property in a certain invention or improvement in

9- SUBSTITUTED MINOCYCLINE COMPOUNDS

described in an application

☐ executed by us of even date herewith and about to be filed

☒ Serial No. 09/895,857, filed on June 29, 2001

in the United States Patent and Trademark Office, and in all Letters Patent of the United States and all foreign countries which may or shall be granted on said invention, or any parts thereof, or on said application, or any divisional, continuing, reissue or other applications based in whole or in part thereon. And I agree, for myself and my executors and administrators, with said corporation and its successors and assigns but at its or their expense and charges, hereafter to execute all applications, amended specifications, deed or other instrument, and to do all acts necessary or proper to secure the grant of Letters Patent in the United States and in all other countries to said corporation, with specifications and claims in such form as shall be approved by the counsel of said corporation and to vest and confirm in said corporation, its successors and assigns, the legal title to all such patents.

And I do hereby authorize and request the Commissioner of Patents and Trademarks of the United States to issue such Letters Patent as shall be granted upon said application or applications based thereon to said corporation, its successors and assigns.

WITNESS my hand and seal this 06 day of March, 2002.

By: David Messersmith  
David Messersmith

Commonwealth of Massachusetts )  
County of Middlesex )ss

Then personally appeared the above named David Messersmith and acknowledged the foregoing instrument to be his free act and deed, before me, this 6 day of March, 2002.

Edmund M. [Signature]  
Notary Public

My commission expires: 4/12/02



We, Mark L. Nelson, of Wellesley, Massachusetts, and Mohamed Y. Ismail, of Bedford, Massachusetts, in consideration of One Dollar and other valuable consideration paid to us by

AND

corporations of Massachusetts and Delaware, respectively, having their respective principal places of business at Ballou Hall, 4<sup>th</sup> Floor, Medford, MA 02155, and 75 Kneeland Street, Boston, MA 02111, the receipt of which is hereby acknowledged, do hereby sell, assign and transfer unto said

AND

their successors and assigns, the entire interest for the United States of America and all foreign countries including all rights of priority under the International Convention for the Protection of Industrial Property in a certain invention or improvement in

described in an application

- ☐ executed by us of even date herewith and about to be filed
- ☒ Serial No. 09/895,857, filed on June 29, 2001

in the United States Patent and Trademark Office, and in all Letters Patent of the United States and all foreign countries which may or shall be granted on said invention, or any parts thereof, or on said application, or any divisional, continuing, reissue or other applications based in whole or in part thereon. And we agree, for ourselves and our executors and administrators, with said corporation and its successors and assigns but at its or their expense and charges, hereafter to execute all applications, amended specifications, deed or other instrument, and to do all acts necessary or proper to secure the grant of Letters Patent in the United States and in all other countries to said corporation, with specifications and claims in such form as shall be approved by the counsel of said corporation and to vest and confirm in said corporation, its successors and assigns, the legal title to all such patents.

And we do hereby authorize and request the Commissioner of Patents and Trademarks of the United States to issue such Letters Patent as shall be granted upon said application or applications based thereon to said corporation, its successors and assigns.

WITNESS my hand and seal this 3<sup>rd</sup> day of OCTOBER, 2001.

By: Mark L. Nelson  
Mark L. Nelson

Commonwealth of Massachusetts )  
County of Norfolk )ss

Then personally appeared the above named Mark L. Nelson and acknowledged the foregoing instrument to be his free act and deed, before me, this 11 day of October, 2001.

Adrianna Ortiz Notary Public  
My commission expires: Nov. 17 2006

WITNESS my hand and seal this 5 day of OCT, 2001.

By: M. Y. Ismail  
Mohamed Y. Ismail

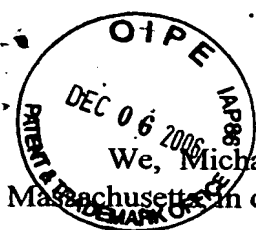
Commonwealth of Massachusetts )  
County of Middlesex )ss  
)

Then personally appeared the above named Mohamed Y. Ismail and acknowledged the foregoing instrument to be his free act and deed, before me, this 11 day of October, 2001.

Adrian Oster  
Notary Public

My commission expires: Nov. 17, 2006

Appendix B  
ASSIGNMENT



We, Michael Draper of Plaistow, New Hampshire and Mark L. Nelson of Wellesley, Massachusetts in consideration of One Dollar and other valuable consideration paid to us by

PARATEK PHARMACEUTICALS, INC.

a corporation of Delaware, having its principal place of business at 75 Kneeland Street, Boston, Massachusetts, the receipt of which is hereby acknowledged, do hereby sell, assign and transfer unto said

PARATEK PHARMACEUTICALS, INC.

its successors and assigns, the entire interest for the United States of America and all foreign countries including all rights of priority under the International Convention for the Protection of Industrial Property in a certain invention or improvement in

SUBSTITUTED TETRACYCLINE COMPOUNDS AS SYNERGISTIC ANTIFUNGAL AGENTS

described in an application

- ☐ executed by us of even date herewith and about to be filed
- ☒ Serial No. 10/097,634, filed on March 14, 2002

in the United States Patent and Trademark Office, and in all Letters Patent of the United States and all foreign countries which may or shall be granted on said invention, or any parts thereof, or on said application, or any divisional, continuing, reissue or other applications based in whole or in part thereon. And we agree, for ourselves and our executors and administrators, with said corporation and its successors and assigns but at its or their expense and charges, hereafter to execute all applications, amended specifications, deed or other instrument, and to do all acts necessary or proper to secure the grant of Letters Patent in the United States and in all other countries to said corporation, with specifications and claims in such form as shall be approved by the counsel of said corporation and to vest and confirm in said corporation, its successors and assigns, the legal title to all such patents.

And we do hereby authorize and request the Commissioner of Patents and Trademarks of the United States to issue such Letters Patent as shall be granted upon said application or applications based thereon to said corporation, its successors and assigns.

WITNESS my hand and seal this 14th day of June, 2002.

By: Michael Draper  
Michael Draper

Commonwealth of Massachusetts )  
County of Suffolk )ss

Then personally appeared the above named Michael Draper and acknowledged the foregoing instrument to be his free act and deed, before me, this 14th day of June, 2002.

Kathleen Williams  
Notary Public

My commission expires: 12-23-05

WITNESS my hand and seal this 14<sup>th</sup> day of June, 2002.

By: Mark L. Nelson  
Mark L. Nelson

Commonwealth of Massachusetts     )  
County of Suffolk                     )ss  
   )

Then personally appeared the above named Mark L. Nelson and acknowledged the foregoing instrument to be his free act and deed, before me, this 14<sup>th</sup> day of June, 2002.

Kathleen Williams  
Notary Public

My commission expires: 12-23-05



Docket No.: PAZ-178CPCN  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Mark L. Nelson *et al.*

Application No.: 10/737,361

Confirmation No.: 6005

Filed: December 15, 2003

Art Unit: 1625

For: AMINO-METHYL SUBSTITUTED  
TETRACYCLINE COMPOUNDS

Examiner: C. C. Chang

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION OF INVENTORS UNDER 37 CFR §1.132**

Dear Sir:

We, Beena Bhatia, Todd Bowser, Laura Honeyman, Mohamed Y. Ismail, and Mark L. Nelson, declare the following:

1. We have reviewed the currently pending claims of the above-referenced application as shown in Exhibit A.
2. We are joint inventors of the invention claimed in Exhibit A, along with Paul Abato, Victor Amoo, Haregewein Assefa, Joel Berniac, Jackson Chen, Roger Frechette, Oak Kim, Rachid Mechiche, Kwasi Ohemeng, N. Laxma Reddy, Atul Verma, Tad Warchol and Ivan Yanachkov.
3. We are aware that the Examiner has rejected claims 16-24 and 26 of the above-referenced application as being anticipated under 35 U.S.C. § 102 (e) by U.S. Patent No. 6,846,939 (the '939 patent'), in which Beena Bhatia, Roger Frechette, Mark L. Nelson and Peter Viski, and are listed as co-inventors.
4. The Examiner's rejection is based on the fact that the '939 patent discloses, but does not claim, the substituted tetracycline compounds shown in Appendix B. These substituted tetracyclines are claimed in the present application, as shown in Exhibit A.
5. We, Beena Bhatia, Todd Bowser, Laura Honeyman, Mohamed Y. Ismail, and Mark L. Nelson, are the inventors of the aforementioned substituted tetracycline compounds described in

the '939 patent and claimed in the present application. Accordingly, these substituted tetracycline compounds are not an invention by another under 35 U.S.C. § 102 (e).

6. We have been warned that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent resulting therefrom. We declare that all of the foregoing statements made of our own knowledge are true and that all statements made on information and belief are believed to be true.

Date: Nov. 29, 2006 Signed: Beena Bhatia  
Beena Bhatia

Date: Nov 29 2006 Signed: Todd Bowser  
Todd Bowser

Date: Nov 29, 2006. Signed: Laura Honeyman  
Laura Honeyman

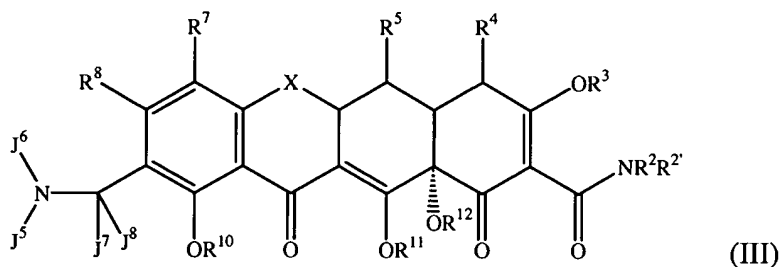
Date: 11-29-06 Signed: Mohamed Y. Ismail  
Mohamed Y. Ismail

Date: Nov 30, 2006 Signed: Mark L. Nelson  
Mark L. Nelson

### Appendix A

1.-15. (Cancelled)

16. A tetracycline compound of formula (III):



wherein:

$J^5$  and  $J^6$  are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, sulfonyl, acyl, alkoxy carbonyl, alkaminocarbonyl, alkaminothiocarbonyl, substituted thiocarbonyl, substituted carbonyl, alkoxythiocarbonyl, or linked to form a ring;

$J^7$  and  $J^8$  are each alkyl, halogen, or hydrogen;

X is  $CR^{6'}R^6$ ;

$R^2$ ,  $R^{2'}$ ,  $R^{4'}$ , and  $R^{4''}$  are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$R^4$  is  $NR^{4'}R^{4''}$ , alkyl, alkenyl, alkynyl, aryl, hydroxyl, halogen, or hydrogen;

$R^3$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each hydrogen or a pro-drug moiety;

$R^5$  is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

$R^6$  and  $R^{6'}$  are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

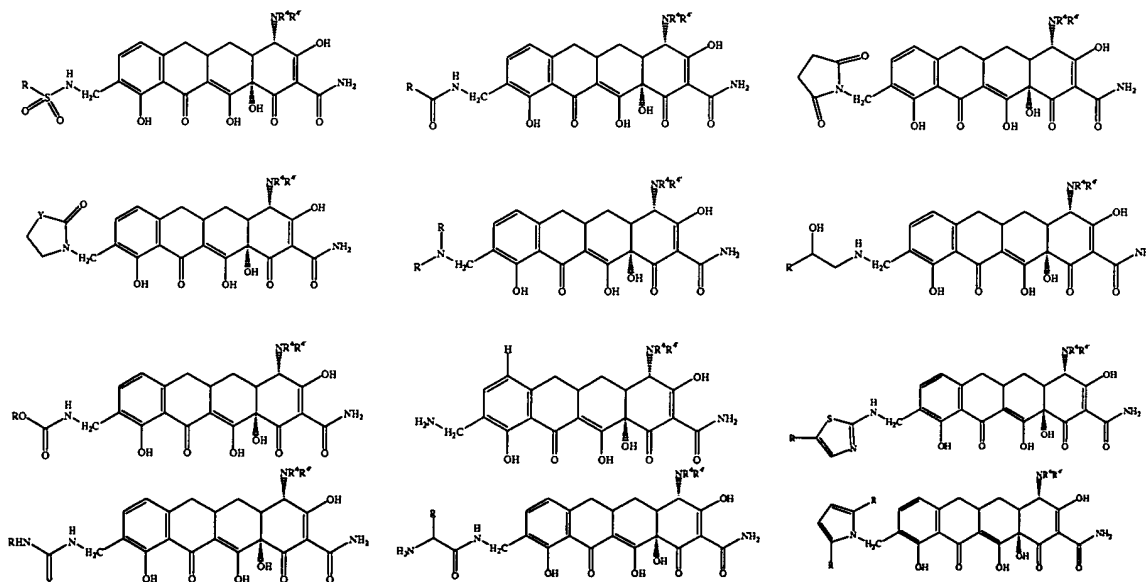
$R^7$  is hydrogen, ethyl, phenyl, 4-*t*-butylphenyl, *t*-butylaminophenyl or dimethylamino;

$R^8$  is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

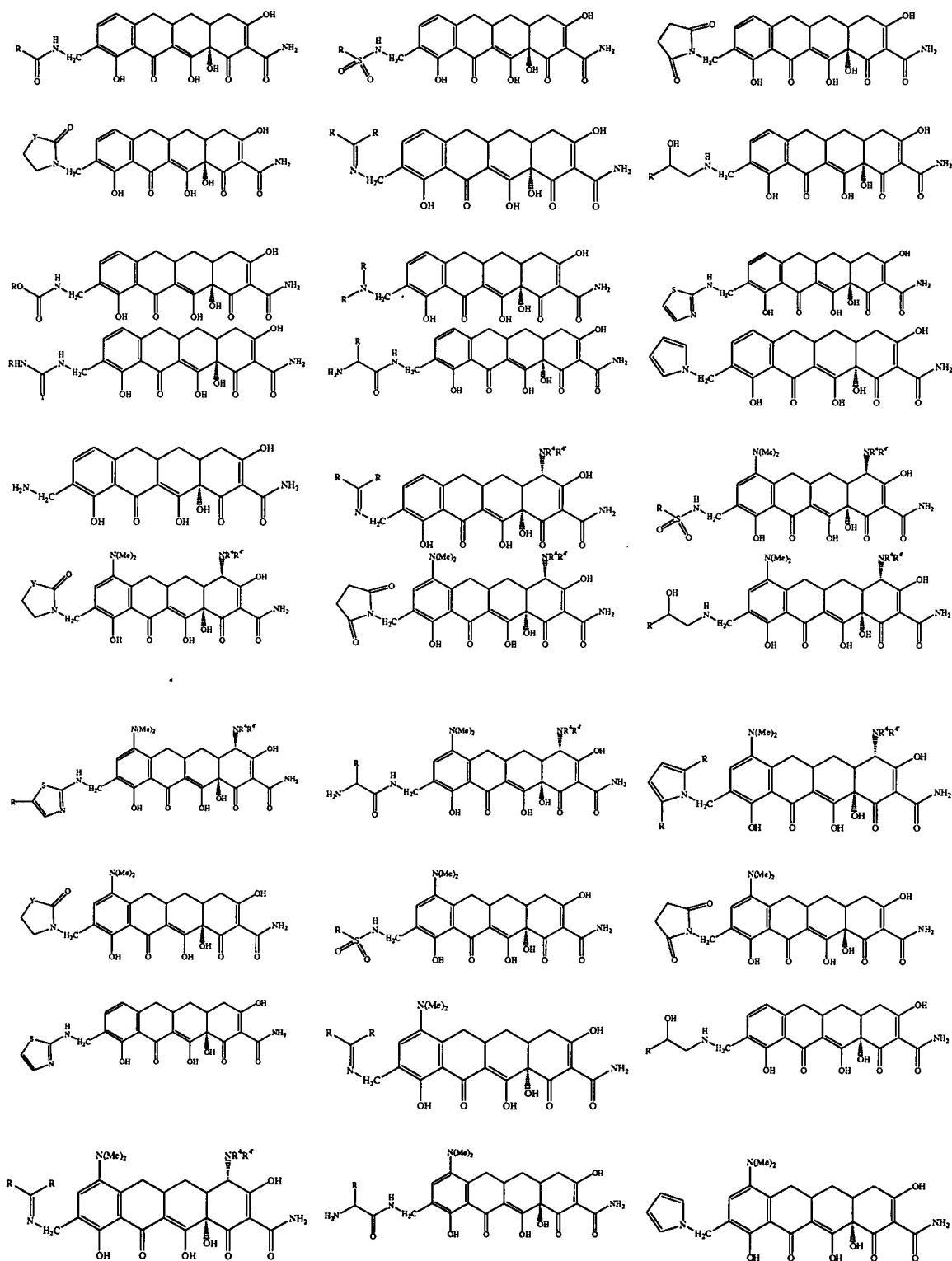
$R^{13}$  is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and

pharmaceutically acceptable salts thereof.

17. The tetracycline compound of claim 16, wherein  $R^4$  is  $NR^{4'}R^{4''}$ , X is  $CR^6R^{6'}$ ;  $R^2$ ,  $R^{2'}$ ,  $R^6$ ,  $R^{6'}$ ,  $R^8$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  are each hydrogen;  $R^{4'}$  and  $R^{4''}$  are lower alkyl; and  $R^5$  is hydroxy or hydrogen.
18. The tetracycline compound of claim 17, wherein  $R^{4'}$  and  $R^{4''}$  are each methyl and  $R^5$  is hydrogen.
19. The tetracycline compound of claim 16, wherein  $J^7$  and  $J^8$  are hydrogen.
20. The tetracycline compound of claim 16, wherein  $J^5$  is substituted or unsubstituted alkyl.
21. The tetracycline compound of claim 16, wherein  $J^5$  is sulfonyl.
22. The tetracycline compound of claim 16, wherein  $J^5$  and  $J^6$  are linked to form a ring.
23. The tetracycline compound of claim 16, wherein  $J^5$  is heteroaryl.
24. The tetracycline compound of claim 16, wherein  $J^5$  is substituted carbonyl.
25. The tetracycline compound of claim 16, wherein said compound is selected from the group consisting of:





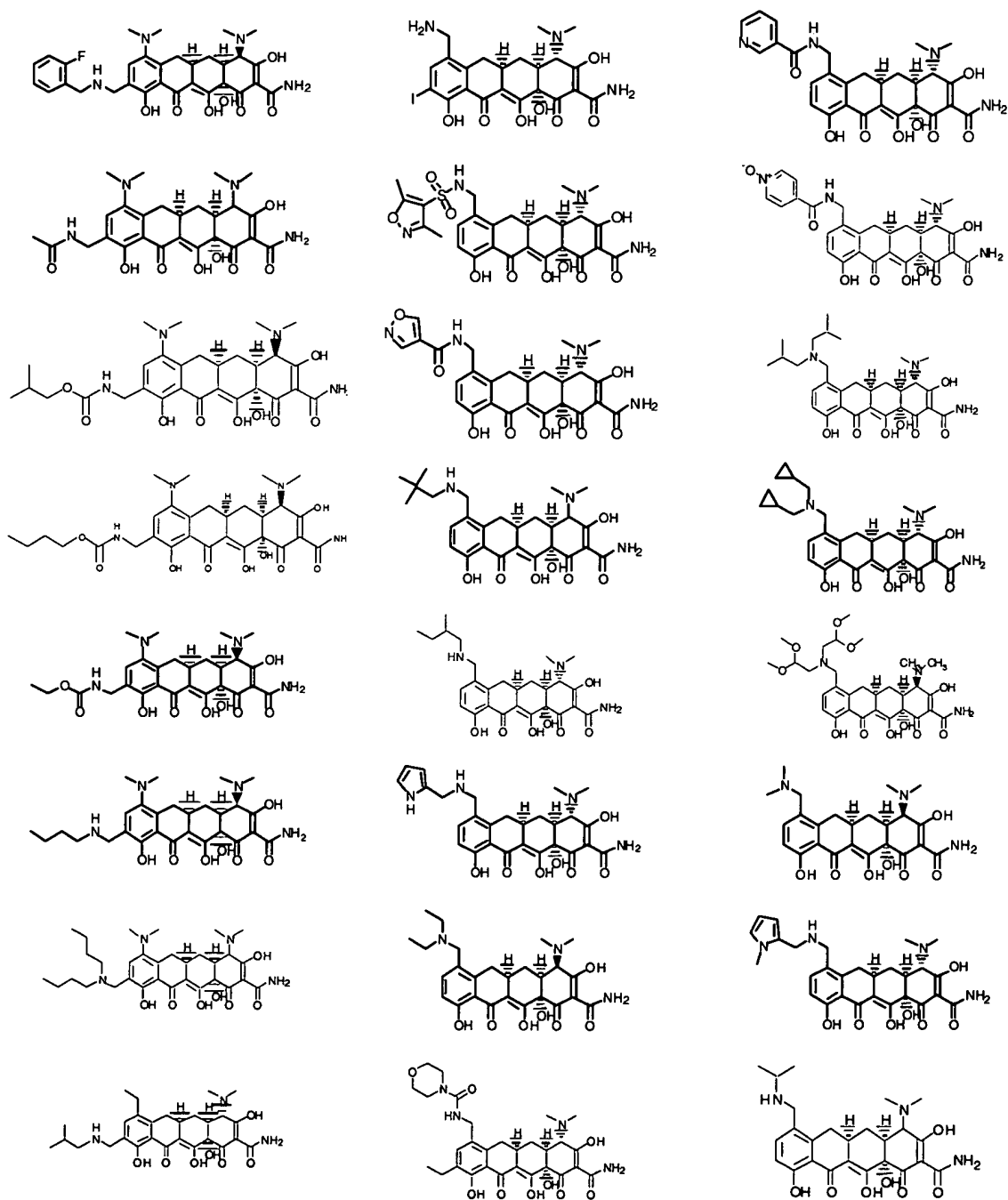


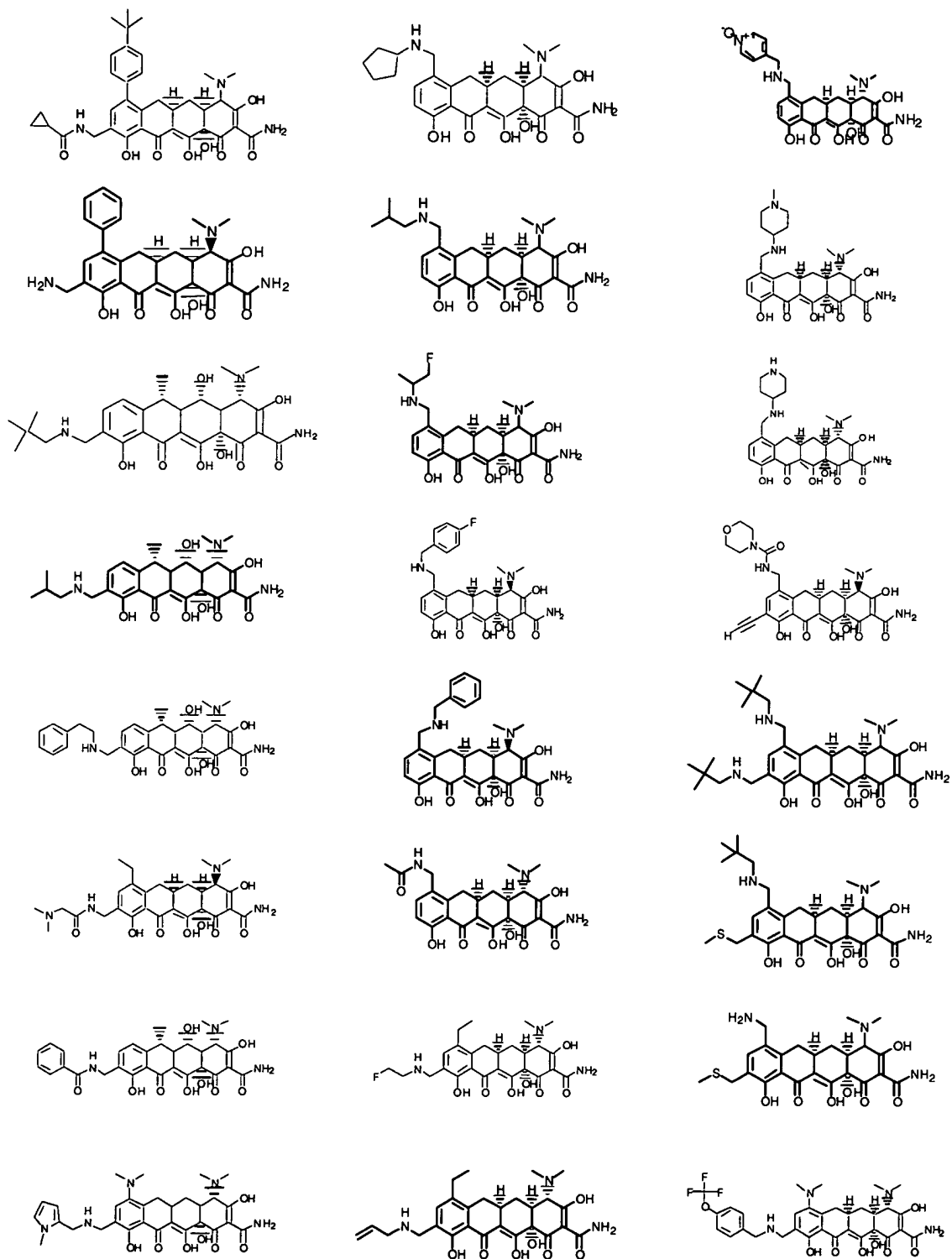
wherein

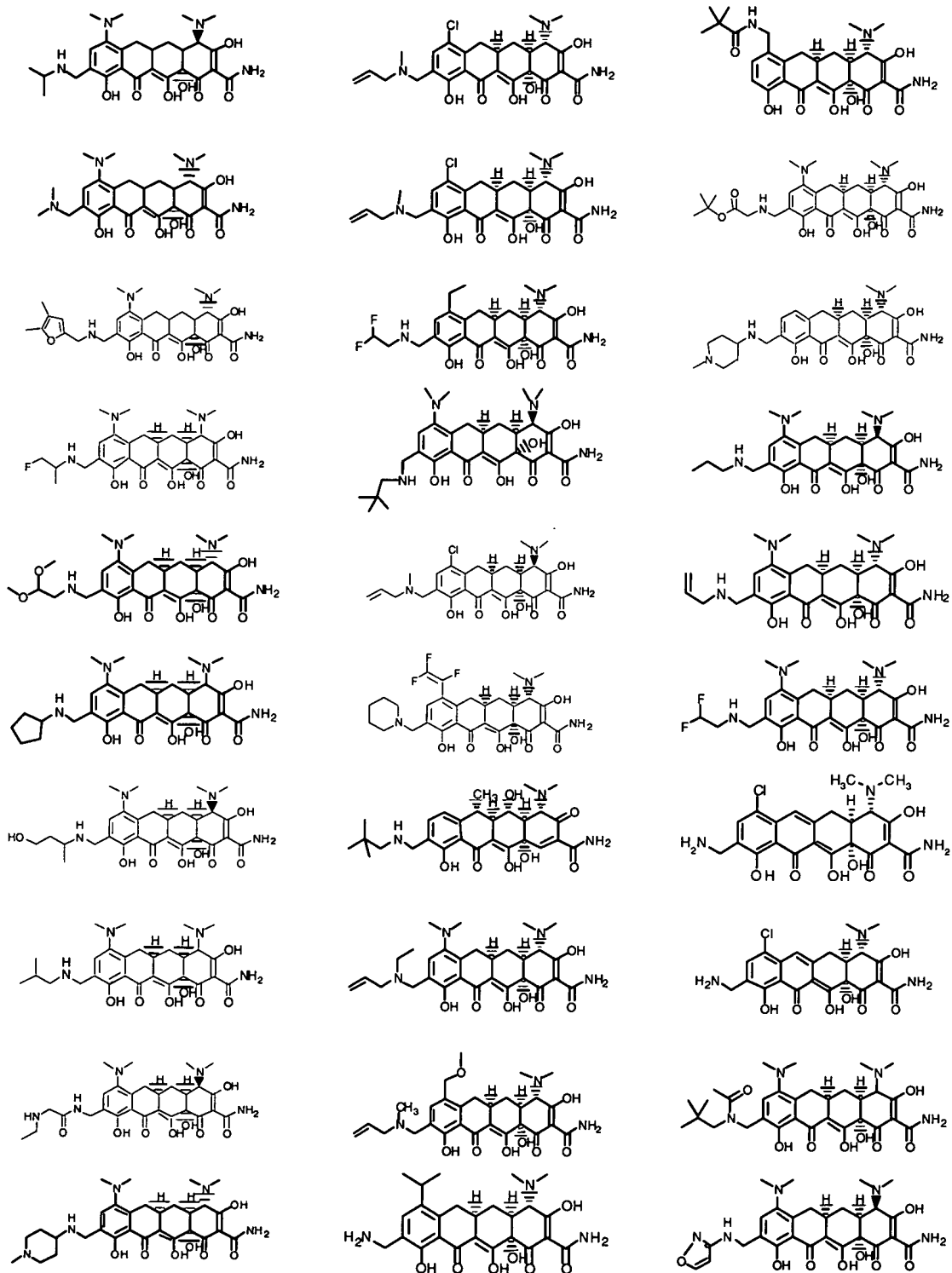
R is substituted or unsubstituted alkyl, alkenyl, alkynyl, halogen, alkoxy; and

Y is N, O, or S, or pharmaceutically acceptable salts or prodrugs thereof.

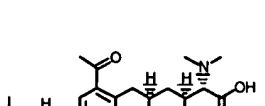
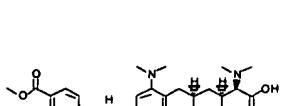
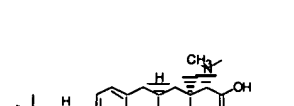
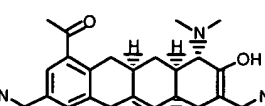
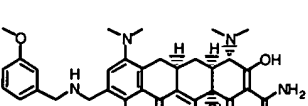
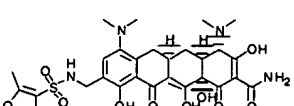
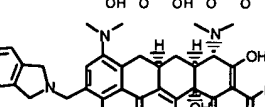
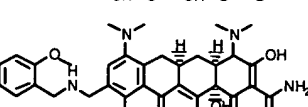
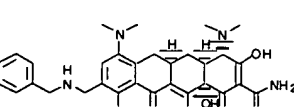
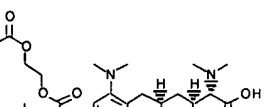
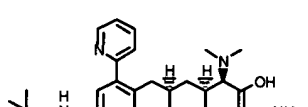
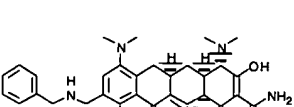
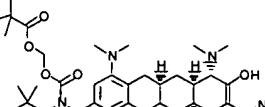
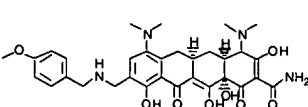
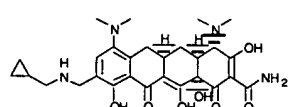
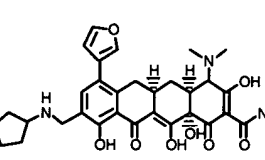
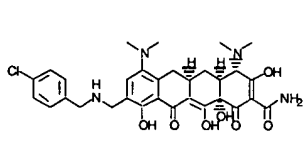
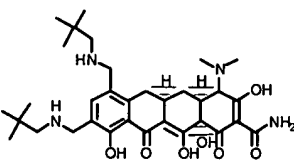
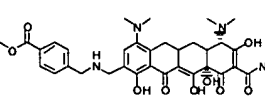
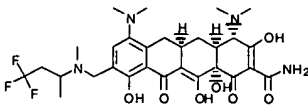
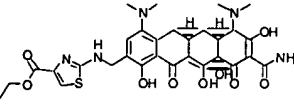
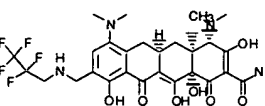
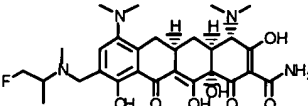
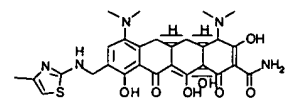
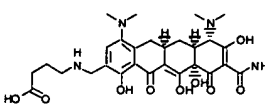
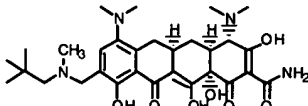
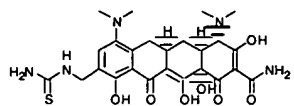
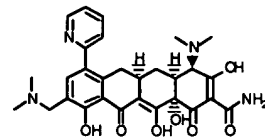
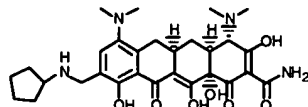
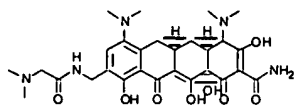
26. A tetracycline compound selected from the following:



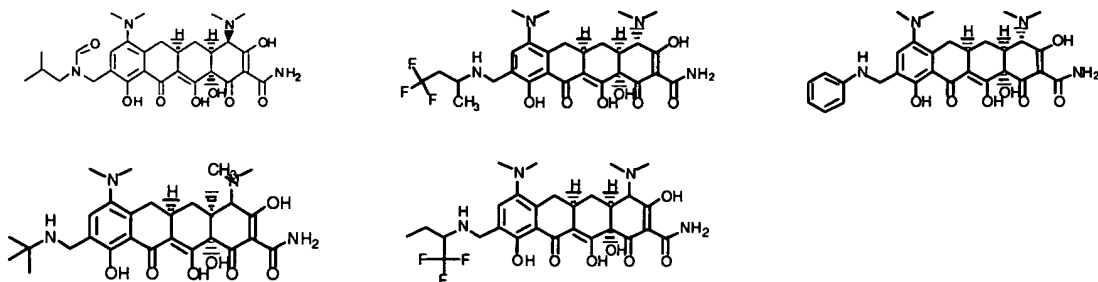












or a pharmaceutically acceptable salt thereof.

27. A pharmaceutical composition comprising an effective amount of a tetracycline compound of any one of claims 16, 25 or 26, and a pharmaceutically acceptable carrier.

28. The pharmaceutical composition of claim 27, wherein said effective amount is effective to treat a tetracycline responsive state.

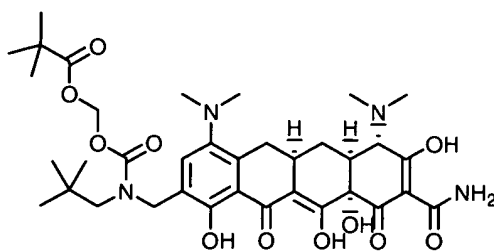
29.-41. (Cancelled)

42. The compound of claim 16, wherein  $R^7$  is dialkylamino.

43. The compound of claim 42, wherein  $R^7$  is dimethylamino.

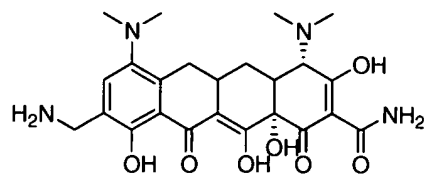
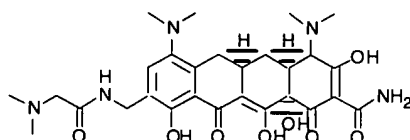
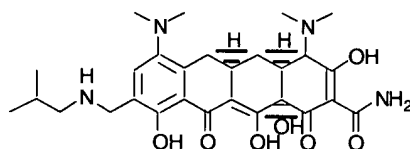
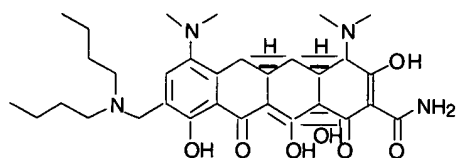
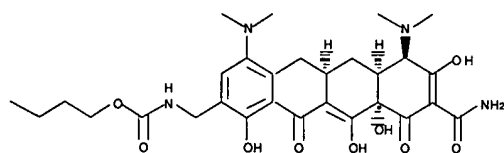
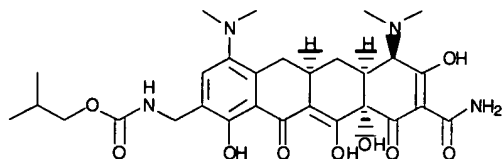
44. The compound of claim 16 or 24, wherein  $J^6$  is alkyl.

45. The compound of claim 44, wherein said compound is





# Appendix B





Docket No.: PAZ-178CPCN  
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:  
Mark L. Nelson *et al.*

Application No.: 10/737,361

Confirmation No.: 6005

Filed: December 15, 2003

Art Unit: 1625

For: AMINO-METHYL SUBSTITUTED  
TETRACYCLINE COMPOUNDS

Examiner: C. C. Chang

MS Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION OF INVENTORS UNDER 37 CFR §1.132**

Dear Sir:

We, Beena Bhatia, Todd Bowser, Jackson Chen, Laura Honeyman, Mohamed Y. Ismail, Mark L. Nelson, Kwasi Ohemeng, N. Laxma Reddy, Atul Verma, Peter Viski, and Ivan Yanachkov, declare the following:

1. We have reviewed the currently pending claims of the above-referenced application as shown in Exhibit A.
2. We are joint inventors of the invention claimed in Exhibit A, along with Paul Abato, Victor Amoo, Haregewein Assefa, Joel Berniac, Roger Frechette, Oak Kim, Rachid Mechiche and Tadeusz Warchol.
3. We are aware that the Examiner has rejected claims 16-24 of the above-referenced application as being anticipated under 35 U.S.C. § 102 (e) by U.S. Patent No. 7,045,507 (the '507 patent'), in which Michael Draper and Mark L. Nelson are listed as co-inventors.
4. The Examiner's rejection is based on the fact that the '507 patent discloses, but does not claim, the substituted tetracycline compounds shown in Appendix B. These substituted tetracyclines are claimed in the present application, as shown in Exhibit A.
5. We, Beena Bhatia, Todd Bowser, Jackson Chen, Laura Honeyman, Mohamed Y. Ismail, Mark L. Nelson, Kwasi Ohemeng, N. Laxma Reddy, Atul Verma, Peter Viski, and Ivan Yanachkov, are the inventors of the aforementioned substituted tetracycline compounds

described in the '507 patent and claimed in the present application. Accordingly, these substituted tetracycline compounds are not an invention by another under 35 U.S.C. § 102 (e).

6. We have been warned that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent resulting therefrom. We declare that all of the foregoing statements made of our own knowledge are true and that all statements made on information and belief are believed to be true.

Date: Nov. 28, 2006 Signed: Beena Bhatia  
Beena Bhatia

Date: Nov 28 2006 Signed: Todd Bowser  
Todd Bowser

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Jackson Chen

Date: Nov 28, 2006. Signed: Laura Honeyman  
Laura Honeyman

Date: NOV. 28, 2006 Signed: Mohamed Y. Ismail  
Mohamed Y. Ismail

Date: Nov 28, 2006 Signed: Mark L. Nelson  
Mark L. Nelson

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Kwasi Ohemeng

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
N. Laxma Reddy

Date: Nov. 28, 2006 Signed: Atul Verma  
Atul Verma

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Peter Viski

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Ivan Yanachkov

described in the '507 patent and claimed in the present application. Accordingly, these substituted tetracycline compounds are not an invention by another under 35 U.S.C. § 102 (e).

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Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Beena Bhatia

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Todd Bowser

Date: 11/29/06 Signed: \_\_\_\_\_  
Jackson Chen

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Laura Honeyman

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Mohamed Y. Ismail

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Mark L. Nelson

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Kwasi Ohemeng

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
N. Laxma Reddy

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Atul Verma

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Peter Viski

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Ivan Yanachkov

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Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
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Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Todd Bowser

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Jackson Chen

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Laura Honeyman

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Mohamed Y. Ismail

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Mark L. Nelson

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Kwasi Ohemeng

Date: 11/29/2006 Signed: N. Laxma Reddy  
N. Laxma Reddy

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Atul Verma

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Peter Viski

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Ivan Yanachkov

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Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Beena Bhatia

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Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
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Mark L. Nelson

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Kwasi Ohemeng

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
N. Laxma Reddy

Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Atul Verma

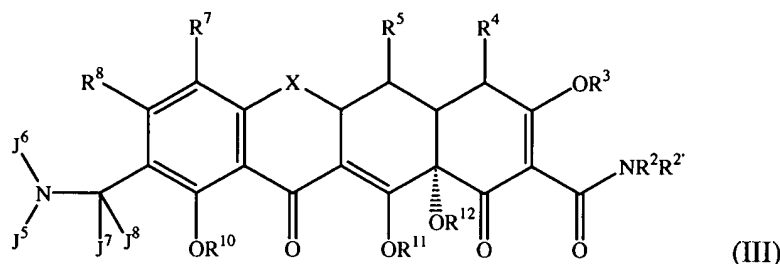
Date: \_\_\_\_\_ Signed: \_\_\_\_\_  
Peter Viski

Date: Dec. 1, 2006 Signed: Ivan Yanachkov  
Ivan Yanachkov

### Appendix A

1.-15. (Cancelled)

16. A tetracycline compound of formula (III):



wherein:

$J^5$  and  $J^6$  are each independently hydrogen, alkyl, alkenyl, alkynyl, aryl, sulfonyl, acyl, alkoxy carbonyl, alkaminocarbonyl, alkaminothiocarbonyl, substituted thiocarbonyl, substituted carbonyl, alkoxythiocarbonyl, or linked to form a ring;

$J^7$  and  $J^8$  are each alkyl, halogen, or hydrogen;

X is  $CR^{6'}R^6$ ;

$R^2$ ,  $R^{2'}$ ,  $R^{4'}$ , and  $R^{4''}$  are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$R^4$  is  $NR^{4'}R^{4''}$ , alkyl, alkenyl, alkynyl, aryl, hydroxyl, halogen, or hydrogen;

$R^3$ ,  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each hydrogen or a pro-drug moiety;

$R^5$  is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

$R^6$  and  $R^{6'}$  are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

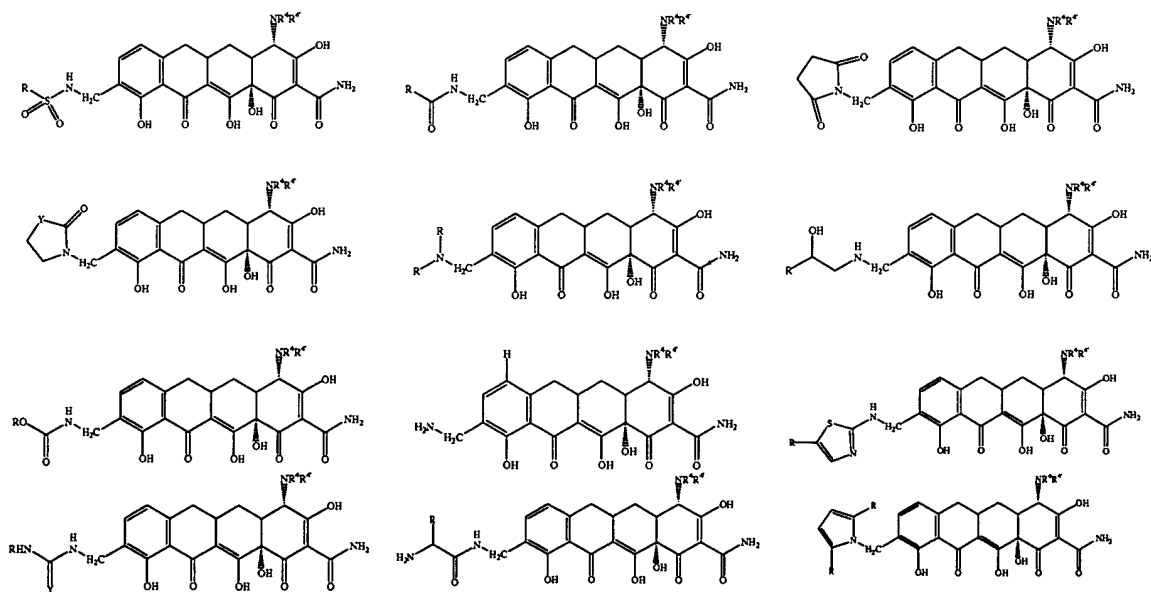
$R^7$  is hydrogen, ethyl, phenyl, 4-*t*-butylphenyl, *t*-butylaminophenyl or dimethylamino;

$R^8$  is hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

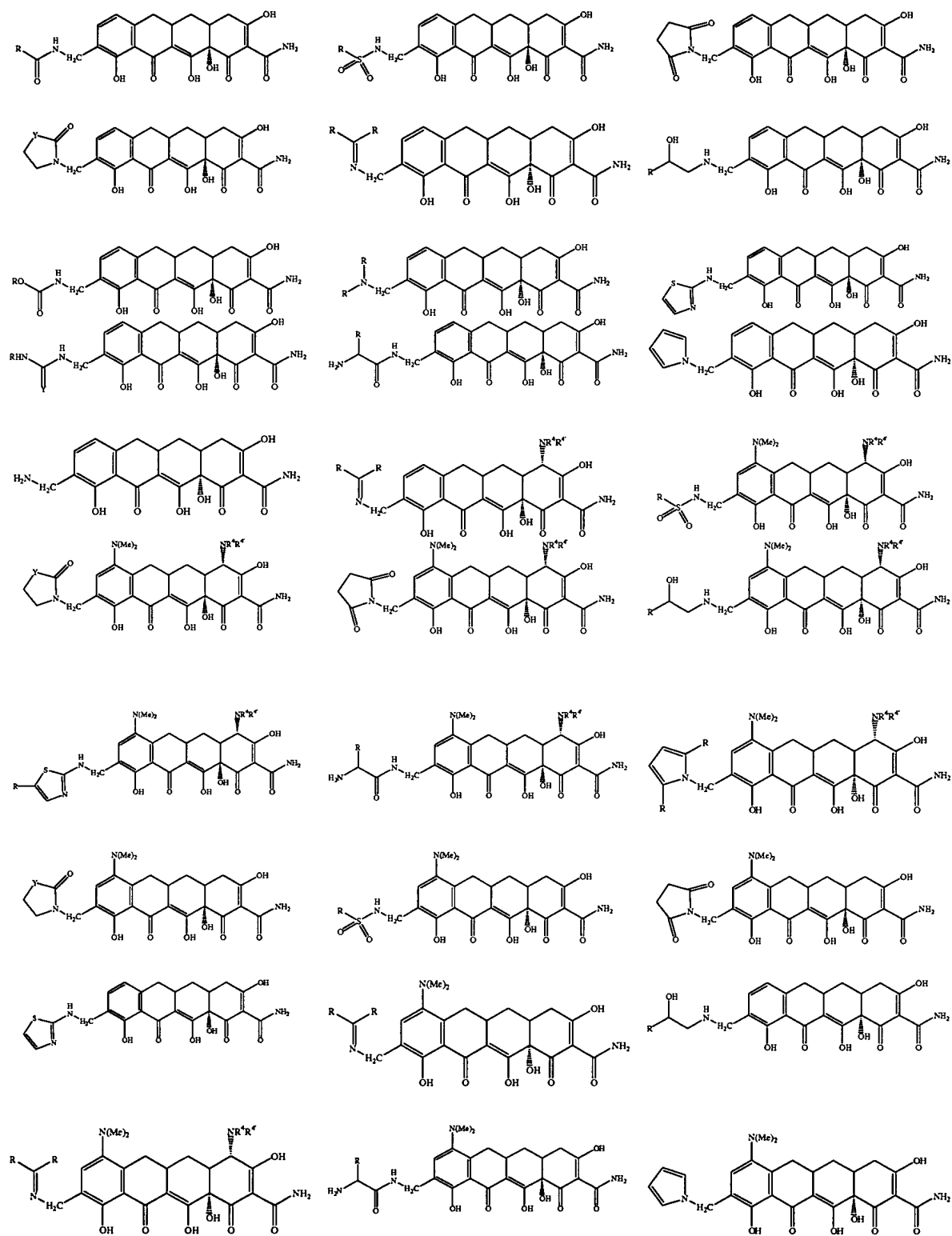
$R^{13}$  is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl; and

pharmaceutically acceptable salts thereof.

17. The tetracycline compound of claim 16, wherein  $R^4$  is  $NR^{4'}R^{4''}$ , X is  $CR^6R^{6'}$ ;  $R^2$ ,  $R^{2'}$ ,  $R^6$ ,  $R^{6'}$ ,  $R^8$ ,  $R^{10}$ ,  $R^{11}$ , and  $R^{12}$  are each hydrogen;  $R^{4'}$  and  $R^{4''}$  are lower alkyl; and  $R^5$  is hydroxy or hydrogen.
18. The tetracycline compound of claim 17, wherein  $R^{4'}$  and  $R^{4''}$  are each methyl and  $R^5$  is hydrogen.
19. The tetracycline compound of claim 16, wherein  $J^7$  and  $J^8$  are hydrogen.
20. The tetracycline compound of claim 16, wherein  $J^5$  is substituted or unsubstituted alkyl.
21. The tetracycline compound of claim 16, wherein  $J^5$  is sulfonyl.
22. The tetracycline compound of claim 16, wherein  $J^5$  and  $J^6$  are linked to form a ring.
23. The tetracycline compound of claim 16, wherein  $J^5$  is heteroaryl.
24. The tetracycline compound of claim 16, wherein  $J^5$  is substituted carbonyl.
25. The tetracycline compound of claim 16, wherein said compound is selected from the group consisting of:





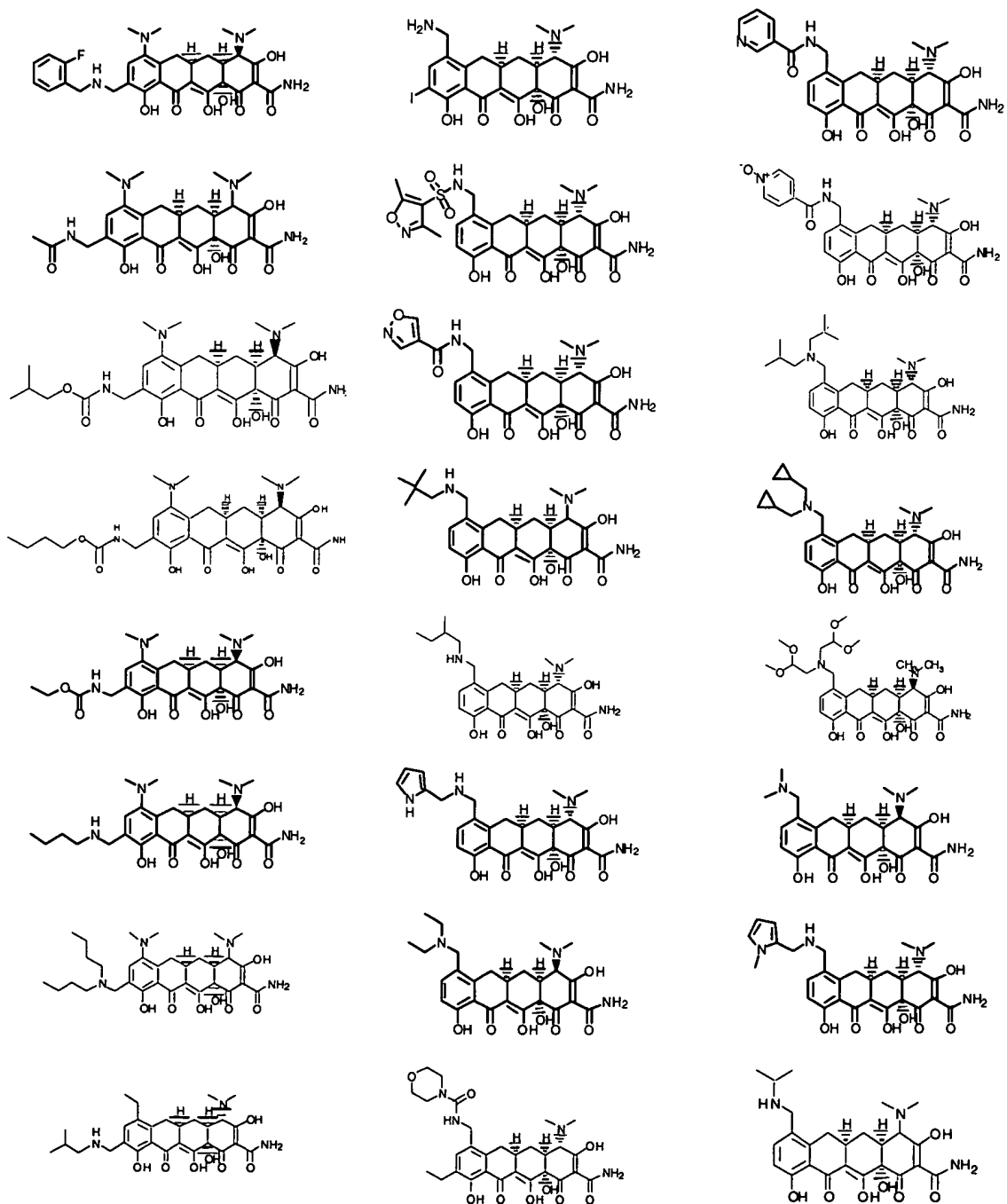


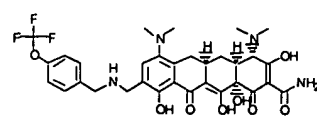
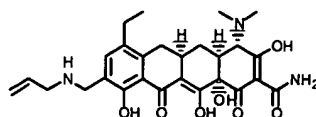
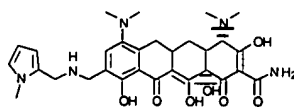
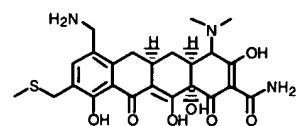
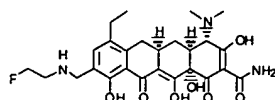
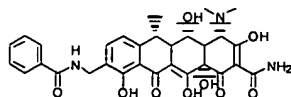
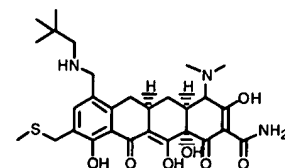
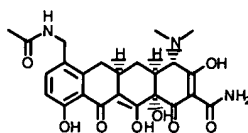
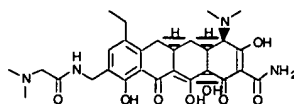
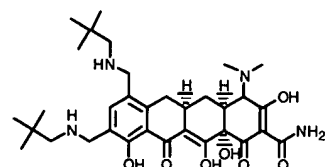
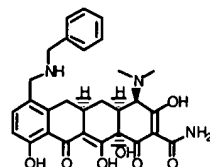
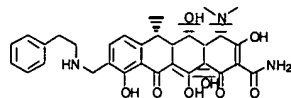
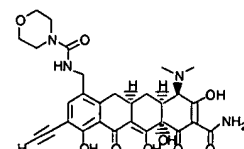
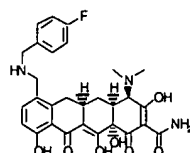
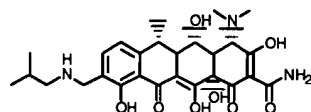
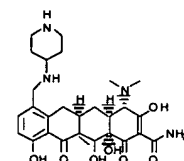
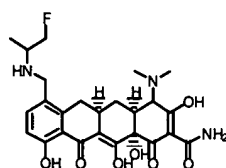
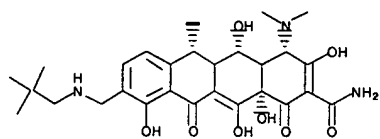
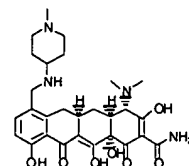
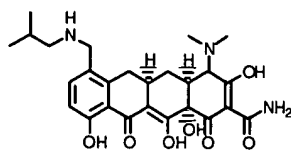
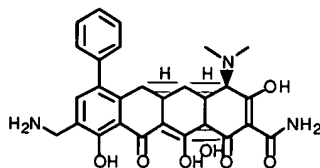
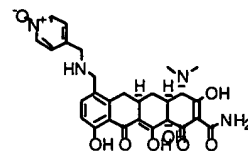
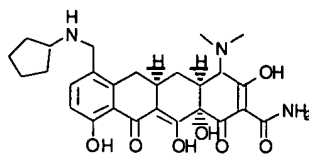
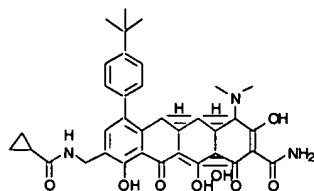
wherein

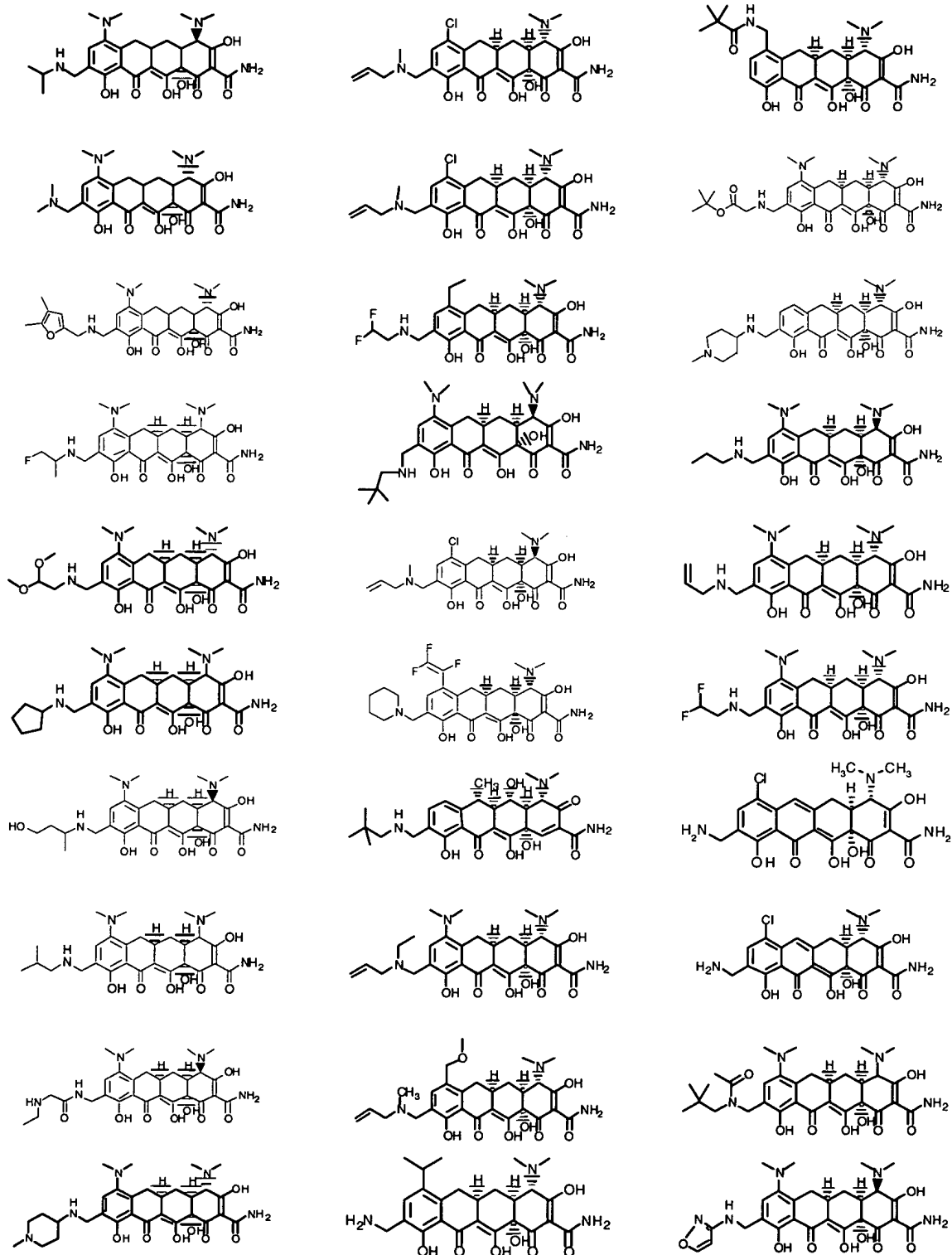
R is substituted or unsubstituted alkyl, alkenyl, alkynyl, halogen, alkoxy; and

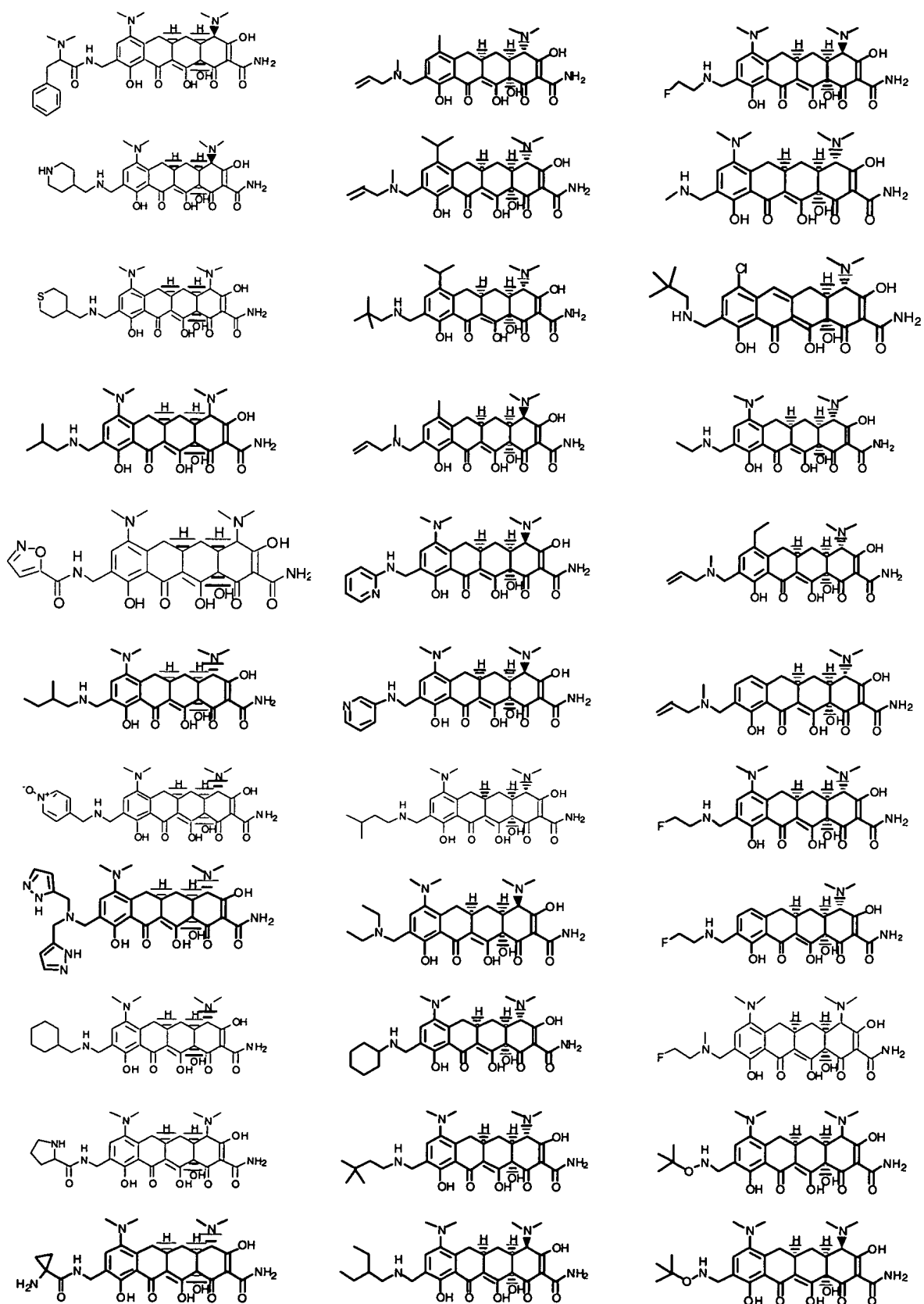
Y is N, O, or S, or pharmaceutically acceptable salts or prodrugs thereof.

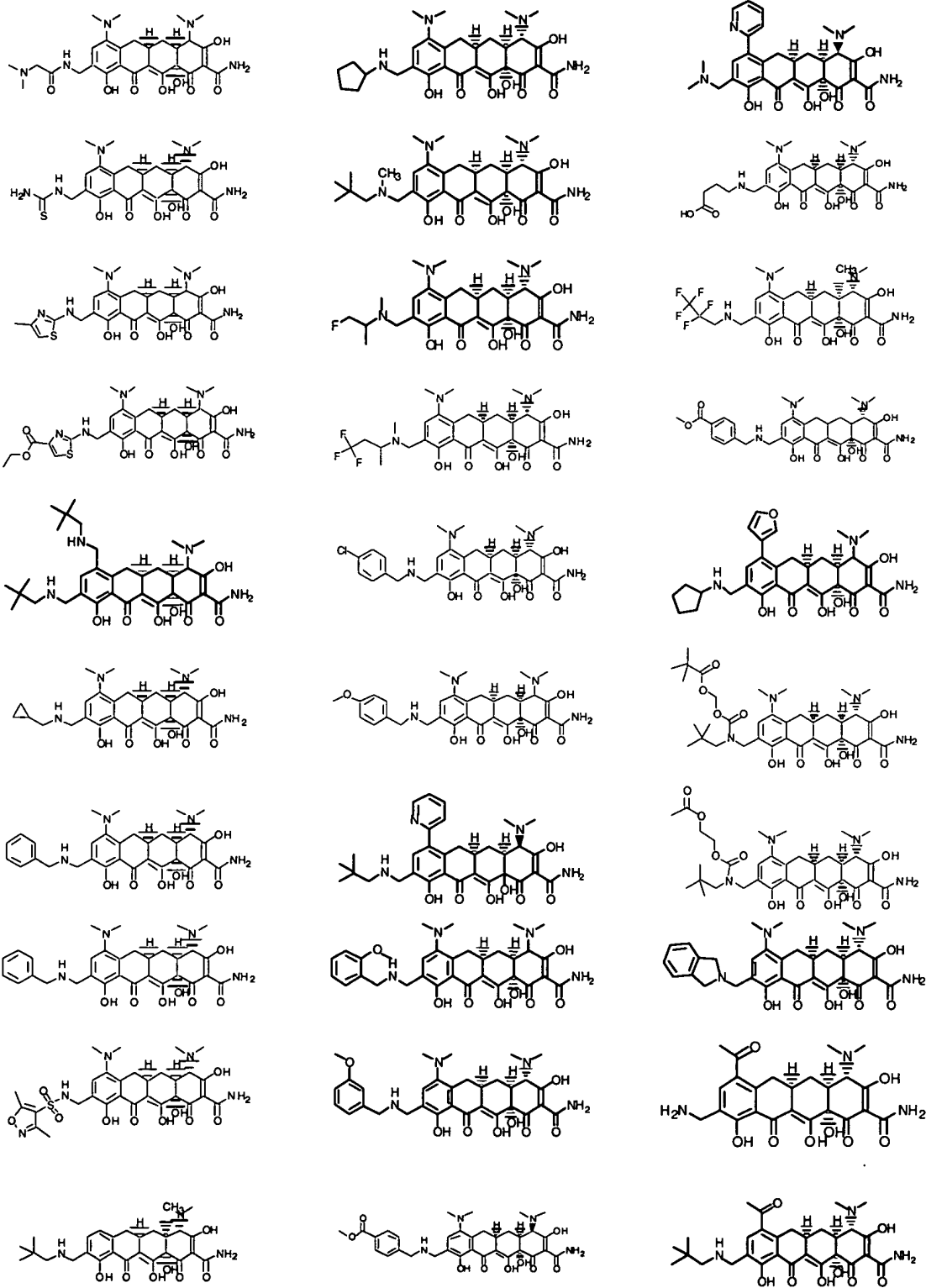
26. A tetracycline compound selected from the following:

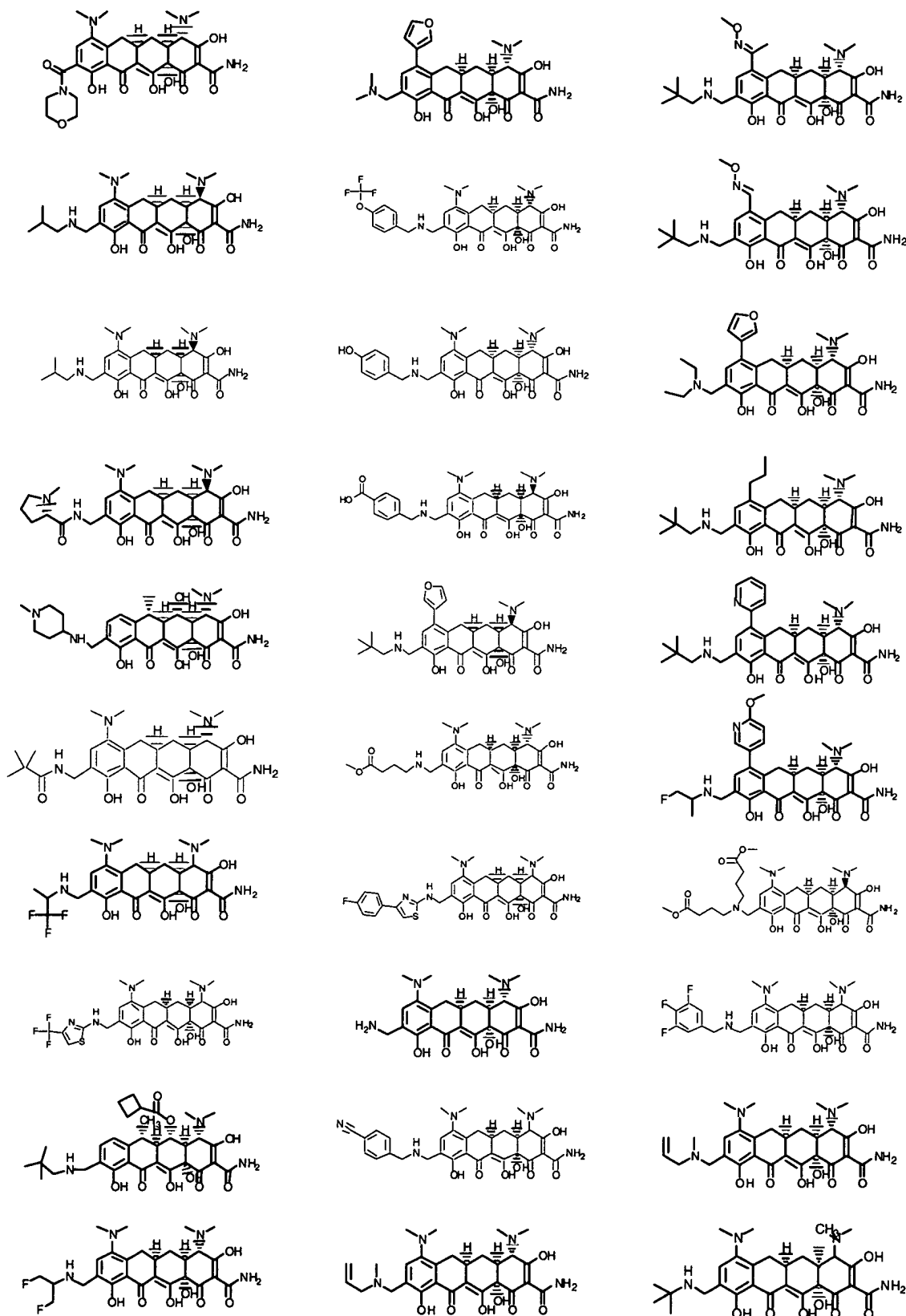


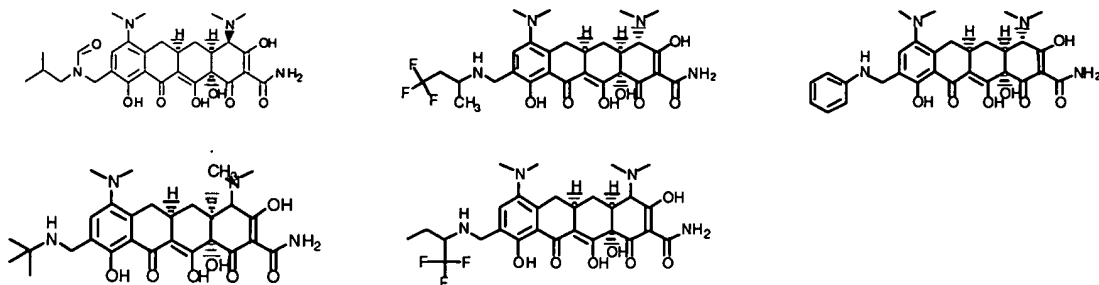












or a pharmaceutically acceptable salt thereof.

27. A pharmaceutical composition comprising an effective amount of a tetracycline compound of any one of claims 16, 25 or 26, and a pharmaceutically acceptable carrier.

28. The pharmaceutical composition of claim 27, wherein said effective amount is effective to treat a tetracycline responsive state.

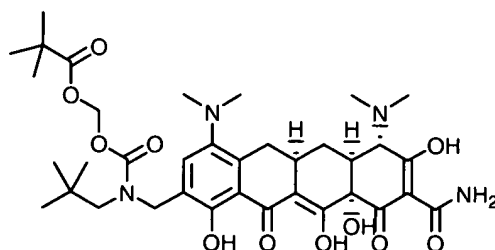
29.-41. (Cancelled)

42. The compound of claim 16, wherein  $R^7$  is dialkylamino.

43. The compound of claim 42, wherein  $R^7$  is dimethylamino.

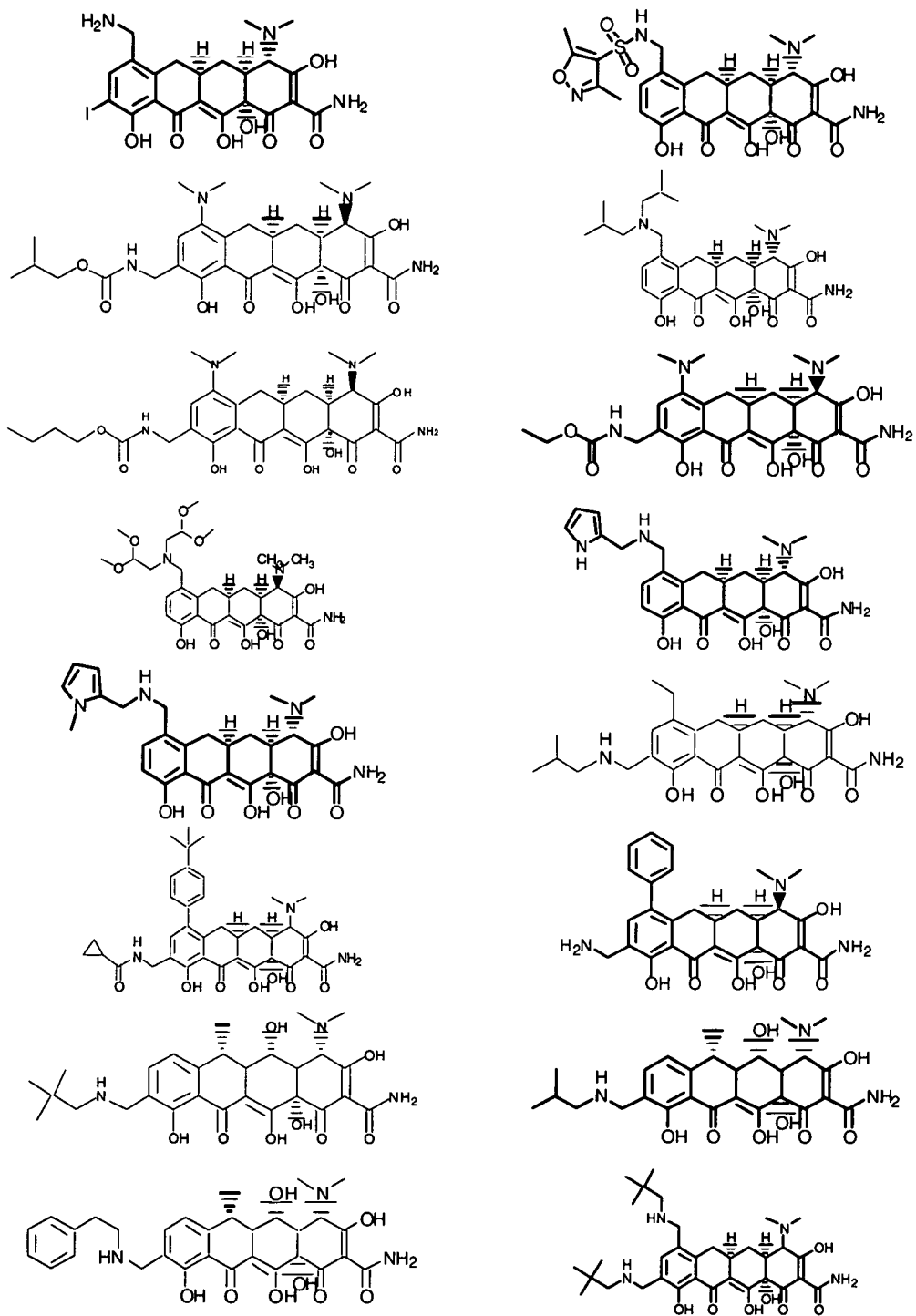
44. The compound of claim 16 or 24, wherein  $J^6$  is alkyl.

45. The compound of claim 44, wherein said compound is





## Appendix B





Application No.: 10/737,361

Docket No.: PAZ-178CPCN

